REMARKS

The foregoing amendments are of a formal nature, and do not add new matter. Claims 39-43 are hereby canceled without prejudice to the filing of a continuation application directed to the canceled subject matter. Claim 44 has been amended to correct a typographical error. Claim 50 has been amended to correct claim dependencies.

Claims 44-46 and 49-51 are currently pending.

Priority Claim

The Examiner acknowledges that applicants have claimed priority to U.S. Provisional Patent Application No. 60/062,816 filed on October 24, 1997. The Examiner has denied the priority claim under 35 U.S.C. 112, because the disclosure regarding PRO246 as a possible virus vector allegedly does not enable one skilled in the art to use the nucleic acid without undue experimentation.

As will be apparent from the discussion below, Applicants submit that the disclosure does provide sufficient information to enable some one skilled in the art to practice the claimed invention. Accordingly the effective filing date of this application is October 24, 1997.

Claims Rejections - 35 U.S.C. §112, first paragraph

Claims 39-43, 50, and 51 stand rejected under 35 U.S.C. §112, first paragraph for alleged lack of enablement.

35 U.S.C. §112, first paragraph requires that an invention be described in such full, clear, concise and exact terms as to enable a person skilled in the art to make and use the same. The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation"" Amgen Inc. v. Hoechst Roussel, Inc. 65 USPQ 2d 1385-1421, 1400 (Fed Cir 2003) citing Genentech, Inc. v. Novo Nordisk, A/S 42 USPQ 2d 1001, 1004 (Fed Cir. 1997). "That some experimentation is necessary does not

constitute a lack of enablement" Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. 18 USPQ 2d 1016, 1026.

The present application, and its earliest priority application 60/062,826 filed on October 24, 1997, provide the nucleic acid and amino acid sequence of the PRO246 polypeptide and indicate that this amino acid sequence shares significant homology to the human Coxsackie-adenovirus receptor. The disclosure further states that a portion of the PRO246 polypeptide has a significant homology with the human cell surface protein HCAR. Considering its significant homology to the human Coxsackie adenovirus receptor, Applicants further suggest the PRO246 polypeptide to be a novel cell surface virus receptor. The specification, at, for example, pages 118-199 and Examples 53-55, provides methods of transforming prokaryotic and eukaryotic cells with the PRO genes and methods of expressing the PRO gene in prokaryotic or eukaryotic cells

It was known in the art at the earliest priority date of the present application that HCAR is a human cellular receptor for the group B Cocksackie-viruses (CVB), and human subgroup C adenoviruses (Ad2 and Ad5) (see Tomko *et al., Proc. Natl. Acad. Sci. USA* 94:3352-3356 (April 1997), a copy of which was previously submitted). In addition, virus assays were well known in the art at the earliest priority date of the present application, as demonstrated. for example, by the disclosure of Tomko *et al., supra*. Such assays could be routinely used at the earliest priority date of the present application to identify the specific viruses that use the PRO246 polypeptide as their receptor. Consequently, based on general knowledge in the art and the disclosure of the present application, at the earliest priority date of the present application one was able to make and use the claimed invention, without undue experimentation.

The Examiner states that the assertion that the PRO246 polypeptide is a virus receptor is unreasonable given the allegedly large degree of divergence between applicant's protein and the most similar known virus. Accordingly, one skilled in the art would not be able to use the PRO246 polypeptide as a receptor for routine virological purposes.

In support of this argument, the Examiner states that alignment of Applicants' sequence with the human and mouse CAR proteins indicates an overall similarity of 17% and a best local similarity of 27%. The Examiner cites McNicholl et al. as evidence that a protein with 100% homology to a portion of a virus receptor does not function as a virus receptor and Struyf et al. that alteration of even a few amino acids degrades the ability of another receptor to interact with virus.

First, Applicants note that both McNicholl et al. and Struyf et al. teach and disclose experiments altering a naturally occurring receptor. They are not comparing two different receptors. If certain alterations are made to a protein it can be rendered inactive. Such papers are not probative of whether a viral receptor must be highly homologous to the CAR receptor in order to be functional.

Second, the Examiner disputes that assays such as those of Tomko et al could be used to identify the specific viruses that use the polypeptide as a receptor and therefore alleges that the patent specification requires undue experimentation.

The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. In re Wands 858 F.2d 731, 737.

Applicants note that Tomko et al. provides a general virus assay on page 3352. Tomko provides a method for transfecting NIH3T3 cells with a plasmid expressing the receptor. Tomko et al. provides a virus assay to be conducted with different viruses on the transformed cells. Clearly such assays could be routinely used at the earliest priority date of the present application to identify the specific viruses that use the PRO246 polypeptide as their receptor.

Finally, the Examiner argues that Applicants cannot rely on U.S. 5,942,606, as prima facie evidence that Applicants' specification is sufficient to teach those skilled in the art to make and use the claimed invention without undue experimentation.

Applicants cite U.S. Patent No. 5,942,606 as evidence that Applicant's specification does not require undue experimentation having due regard for the nature of the invention and the state of the art. The Examiner clearly declares that U.S. Patent No. 5,942,606 is fully enabled because the Examiner is citing U.S. Patent No. 5,942,606

against the Applicant as 102(e2) prior art. "To serve as an anticipating reference, the reference must enable that which it is asserted to anticipate. "A claimed invention cannot be anticipated by a prior art reference if the allegedly anticipatory disclosure cited as prior art is not enabled"" See Elan Pharmaceuticals, Inc. and Athena Neurosciences, Inc. v. Mayo Foundation for Medical Education and Research 2003 U.S. App Lexis 20195 (Fed Cir 2003) citing Amgen, Inc. v. Hoechst Marion Roussel, Inc. 314 F.3d 1313, 1354, 65 USPQ 2d 1385, 1416 (Fed. Cir. 2003). U.S. Patent No. 5,942,606 discloses a protein designated ACVRP, which is identical with the PRO246 polypeptide of the present application, and provides a very similar disclosure to the current specification. It simply provides sequence homology with HCAR as support for the sequence being useful as a viral receptor. The specification of the issued U.S. patent is devoid of any experimental data demonstrating the antiviral activity of ACVRP, or identifying the specific viruses associated with this receptor. Accordingly, if U.S. 5,942,606 is fully enabled, Applicants currently claimed invention is similarly fully enabled. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claims 39-43, and 50-51 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification as to reasonably convey that the inventors had possession of the claimed invention at the time the application was filed. The Examiner objects to the phrase "wherein said polypeptide is a viral receptor". The Examiner alleges that the specification provides no reason to believe that the PRO246 sequence fragments and variants function as a viral receptor.

This rejection is traversed by Applicants cancellation of Claims 39-43 without prejudice to filing a continuation application directed to the canceled subject matter and Applicants amendment of Claim 50 to change the claim dependencies.

Claim Rejections - 35 USC §102

Claims 39-46, and 49-50 were rejected under 35 USC §102(e2) "as being anticipated by Lal et al. 5,942,606."

As discussed above, the present application is entitled to the priority date of October 24, 1997, which precedes, by one month, the earliest priority date of Lal et al. (November 24, 1997). Accordingly, Lal et al. is not prior art against the present application, and the present rejection should be withdrawn.

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should the Examiner find that there are any further issues outstanding, she is invited to contact the undersigned attorney at the telephone number shown below.

It is emphasized that all amendments made herein are without prejudice, and without acquiescing to any of the rejections raised in the Office Action of May 20, 2003, or any reasoning underlying the rejections. The sole purpose of the present amendments is to facilitate the prosecution of the present application. Applicants specifically retain the right the pursue any subject matter not literally covered by the current claims in any or more continuing applications.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-1618 P2C21**).

Respectfully submitted,

Date: October 14, 2003

Leslie A. Mooi (Reg. No. 37,047)

HELLER EHRMAN WHITE & McAULIFFE LLP
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

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